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ELECTRODES FOR FUNCTIONAL ELECTRICAL STIMULATION

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Principal Investigator
J. Thomas Mortimer, Ph.D.

Applied Neural Control Laboratory
Department of Biomedical Engineering
Case Western Reserve University
Cleveland, OH USA

TABLE OF CONTENTS

SECTION B. DESIGN AND FABRICATION OF ELECTRODES, LEADS AND CONNECTORS

B.2.1.2 Polymer-Metal Foil-Polymer (PMP) Cuff Electrodes

In order to characterize the laser machined structure in the polymer-metal foil-polymer electrode, simple versions of the platinum serpentine structure were created and tensile tested. These structures were basic serpentine paths with a height of 1 mm, a thickness of 0.1 mm and a spacing of 0.2 mm. These are the same dimensions as the basic loop pattern in the current PMP electrode design. One, two and five path structures were manufactured to determine if the addition of paths had an additive effect on the spring constant. Since the stiffness of the platinum is an important variable to minimize in the cuff fabrication process, this test provided insight into the stiffness added by the basic serpentine conductor design. One of each of the one, two, and five path structures were tensile tested. Another set of one, two, and five path structures were laminated and then tensile tested. A set of the 50μm thick MED-4550 silicone rubber sheeting, which was used in the lamination of the structures, were also tensile tested. The graph of the tensile curves for each sample was reported in PR#10. In the current reporting period, extra available samples were tensile tested to increase the sample size of the data. The new graph with the added tensile curves is shown in the figure below.

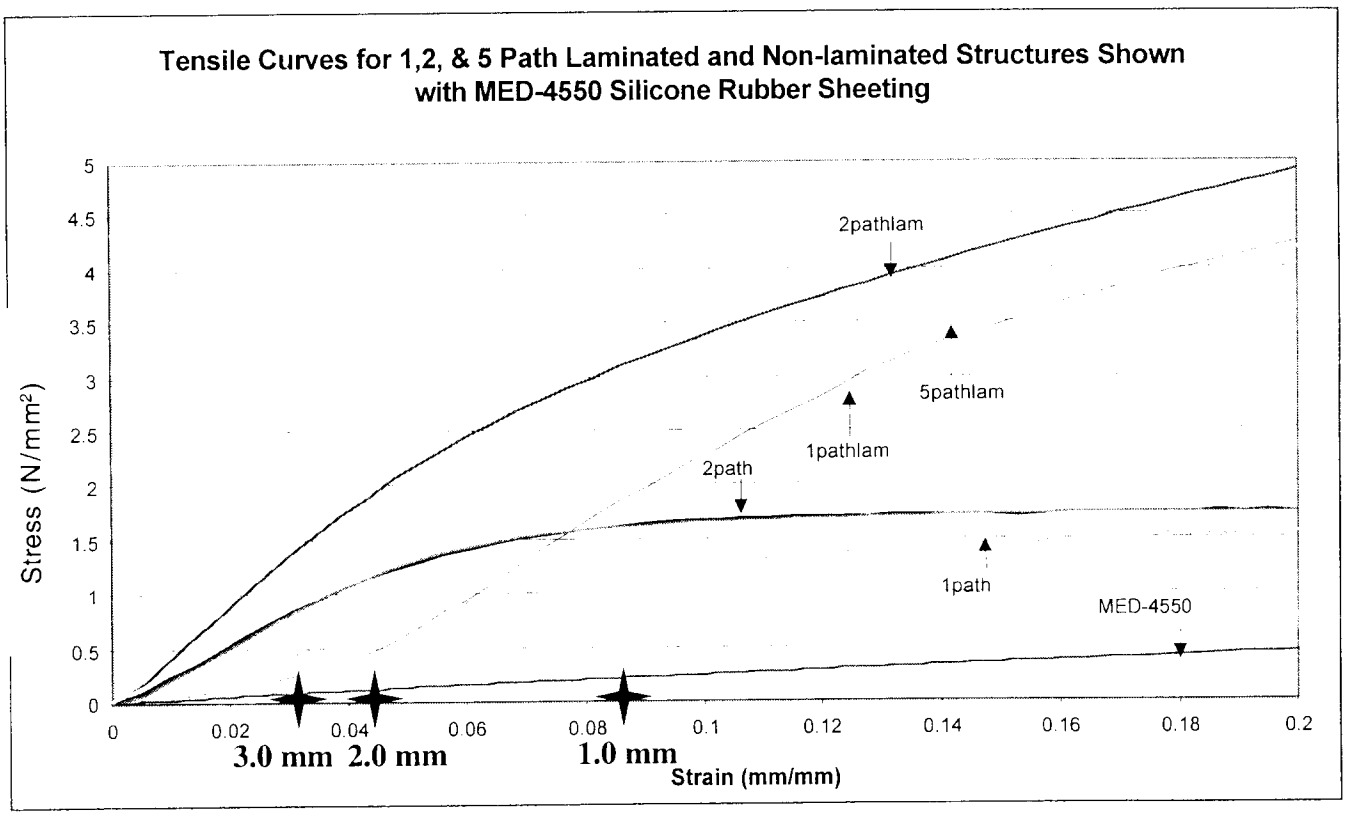

Figure B.1: This graph represents the predicted range of tensile movement for the components within a manufactured 1.0mm,2.0mm, and 3.0mm inner diameter polymer-metal foil-polymer self-sizing spiral cuff electrode. The data extends beyond the region

shown. The maximum estimated strain that the platinum structure may undergo during manufacture is shown on the graph by the stars for a 3.0, 2.0, and 1.0mm cuff electrode.

The region shown in the graph above represents the expected strain materials would have to accommodate when the cuff curls. The expected strain was calculated by assuming that curling was accommodated by stretching the outside of the cuff. Calculations were performed in PR#10 placing the neutral axis on the extreme edges of the cuff thickness. The maximum movement is seen when the neutral axis is on the inside edge of the stretched layer of the cuff.

The slopes of the elastic regions of the tensile curves were analyzed to test the hypothesis that the mechanical properties are additive as the number of paths is increased. The average Young's Modulus (E) for the three laminated structures was 42.35, and for the non-laminated structures it was 31.42. The average E for two sheets of silicone rubber plus one layer of elastomer (approximated as three sheets of silicone) was 11.79. Adding 11.79 and 31.42 yields 43.21. It then appears that the Young's Modulus of the laminated structure is approximately the modulus of the non-laminated structure plus the modulus of two sheets of silicone rubber sheeting plus a layer of elastomer. This analysis was also performed in PR#10 when only one sample per structure type had been tested. In this last period, more samples were added for the structures and the Young's Modulus of the laminated structure is much closer to the Modulus achieved using the additive hypothesis.

Cross-Sectional Views

One PMP3 electrode was laser cut at particular locations to look at the cross-sectional views of the electrode. Scanning Electron Microscopy (SEM) was performed on the edges of fifteen pieces of the electrodes. The SEM pictures showed good adhesion between components and that the elastomer/adhesion does fill in the cavities of the electrode during manufacture.

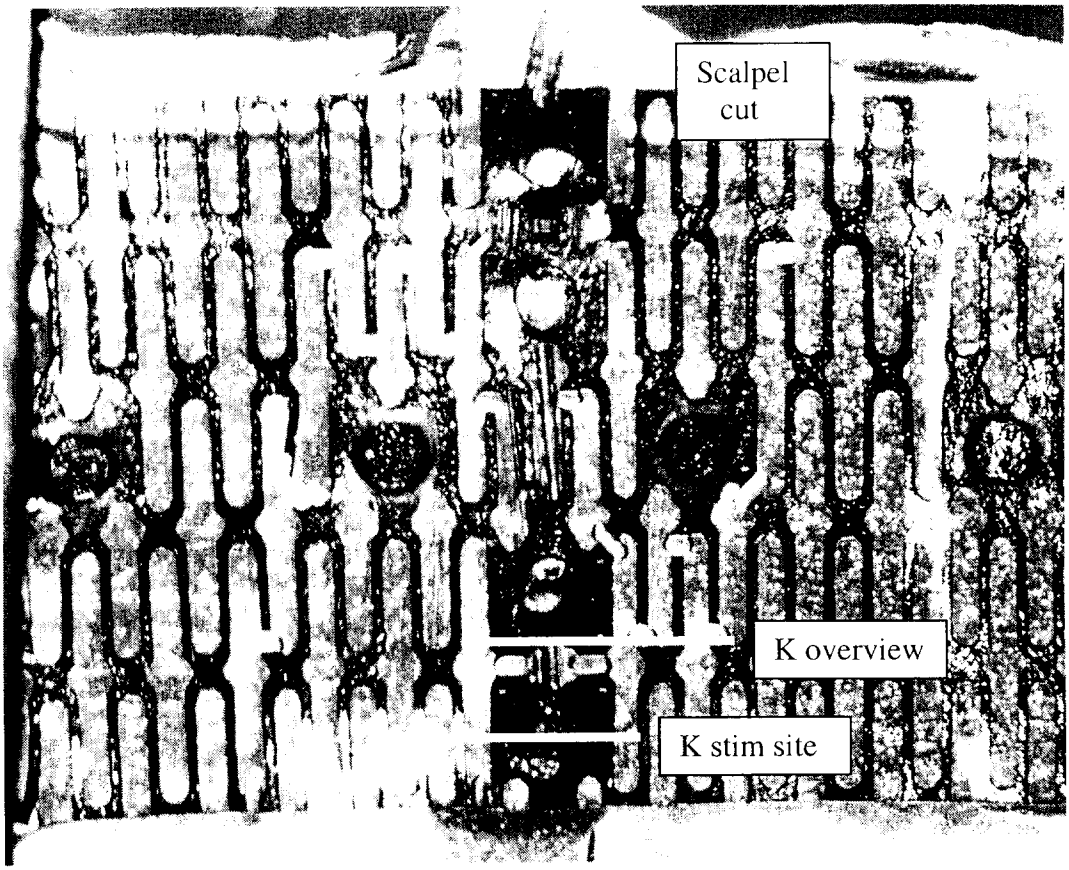

Figure B.2: Picture of the electrode sectioned to investigate the cross-sectional view of various parts of the electrode. The white lines indicate the place of some of the cuts whose edges are presented in the figures below. The top line is an edge that was cut using a scalpel blade. The "K overview" cut was one of the edges of the SEM sampled termed K that shows a cut through several components and the lead wires. The "K stim site" is a view of one of the stimulation sites.

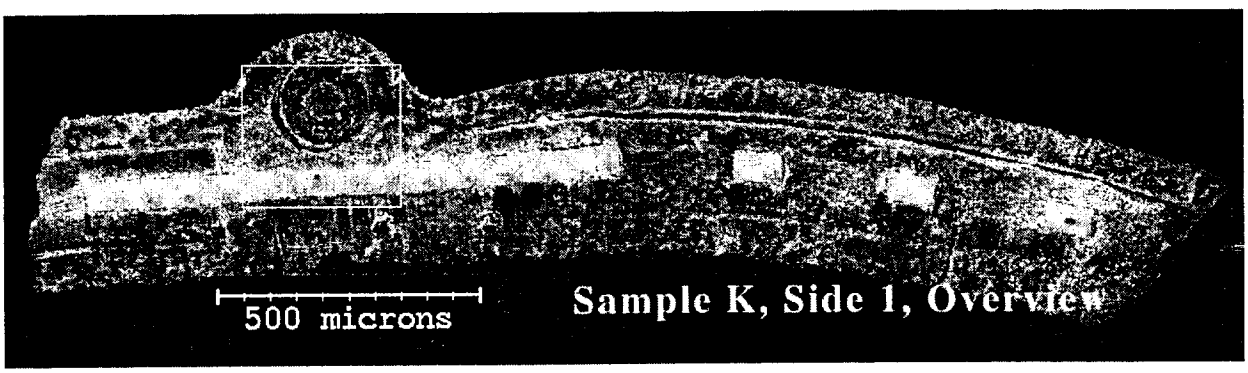

Figure B.3: SEM picture of the edge of the "K overview" cut as seen in Figure B.2. All of the cavities that were created for conduction isolation were filled by adhesive. All of the separate layers can be seen.

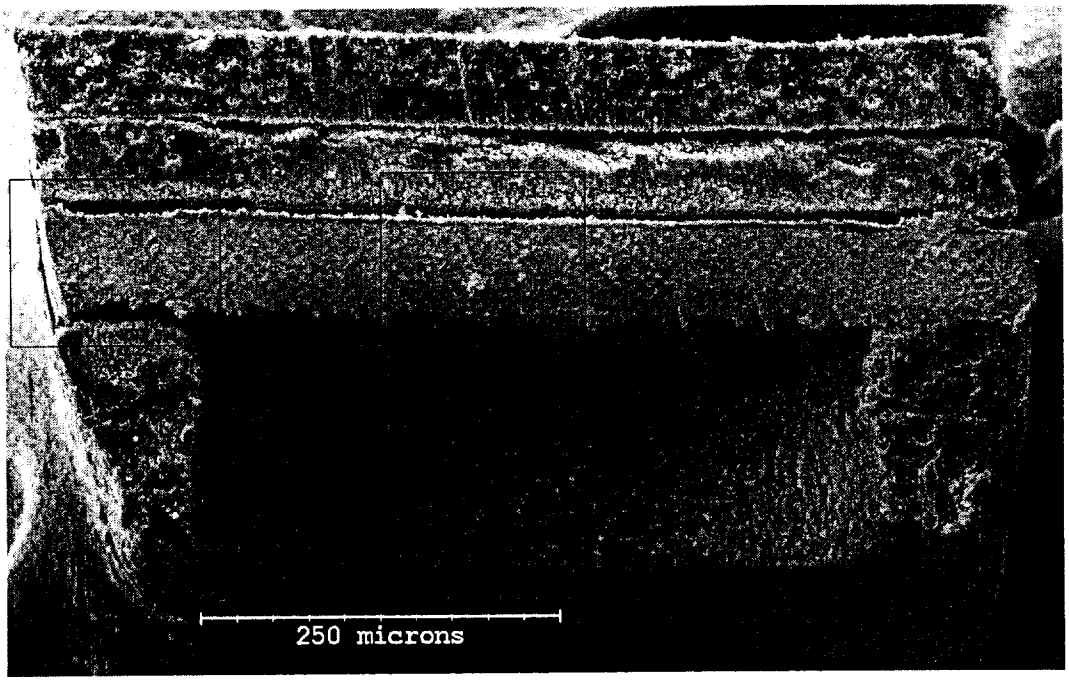

Figure B.4: SEM picture of the edge of cut "K stim site" as seen in Figure B.2. The separate layers can be seen, as well as the clean removal of the silicone pad that was covering the stimulation site.

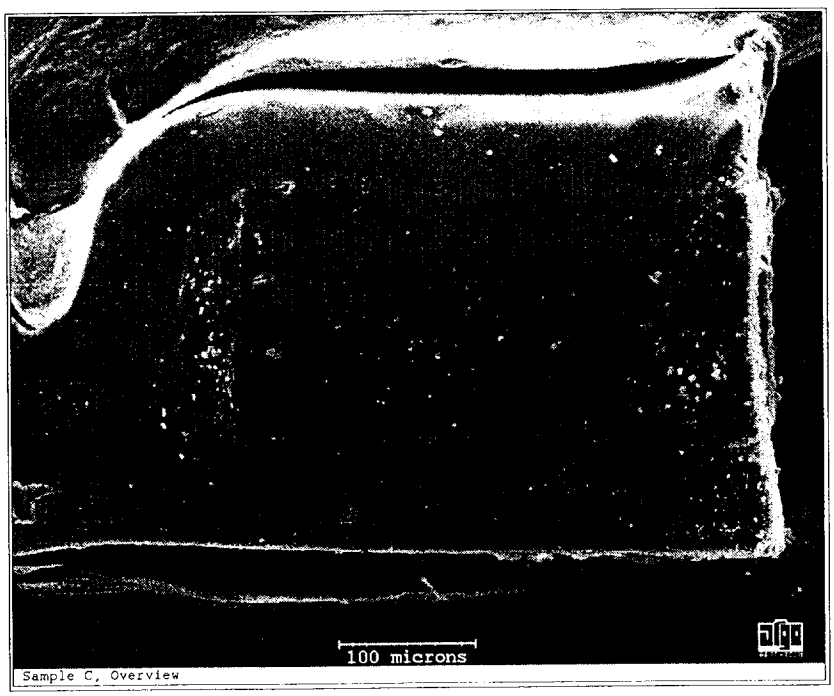

Figure B.5: SEM picture of the edge of cut "scalpel cut" as seen in Figure B.2. This picture was taken to compare with the edges cut by the laser. The laser cut edges show layer separation where the scalpel cut edge shows good adhesion between all layers.

B.2.5.2 Corrosion Testing

Two sets of four electrodes are being tested for corrosion. One set contains electrodes that have undergone simulated aging. These are the four electrodes tested in the Simulated Aging/ Flexion test of Section B.2.5.1. The other set contains two electrodes that were used in the rolling test (Section B.2.5.1). These samples represent electrodes that have been flexed beyond what is expected during manufacture and implant. They will provide information on the relationship between fatigue from flexion and corrosion. The remaining two samples are unused, meaning they have not been flexed, aged, or tested since manufacture.

Results

As reported in PR#10, one batch of four electrodes completed the 28-day test. Two of the electrodes tested had gone through the rolling test, and two were unused. Absorption testing for platinum in solution revealed that there was no platinum loss within the reported detection limit for any of the electrodes. Visual and scanning electron microscopy were also performed on the stimulation sites of the electrode to compare the stimulation sites after stimulation with the control pictures taken of sites that had not been stimulated. There were no noticeable changes in the stimulation site pictures between the control and stimulated sites.

Potential measurements were taken for each stimulation site every three to four days during the 28-day test. The potential recorded was the resting potential as illustrated by the double-sided arrow in the figure below. The average potential measurements for each electrode are shown in Figure B.7.

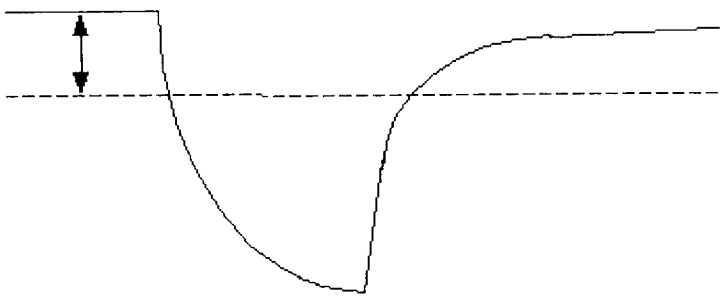

Figure B.6: Representation of the potential measurement for each stimulation site. A total of eight measurements were taken. The "resting" potential indicated by the double-sided arrow was recorded.

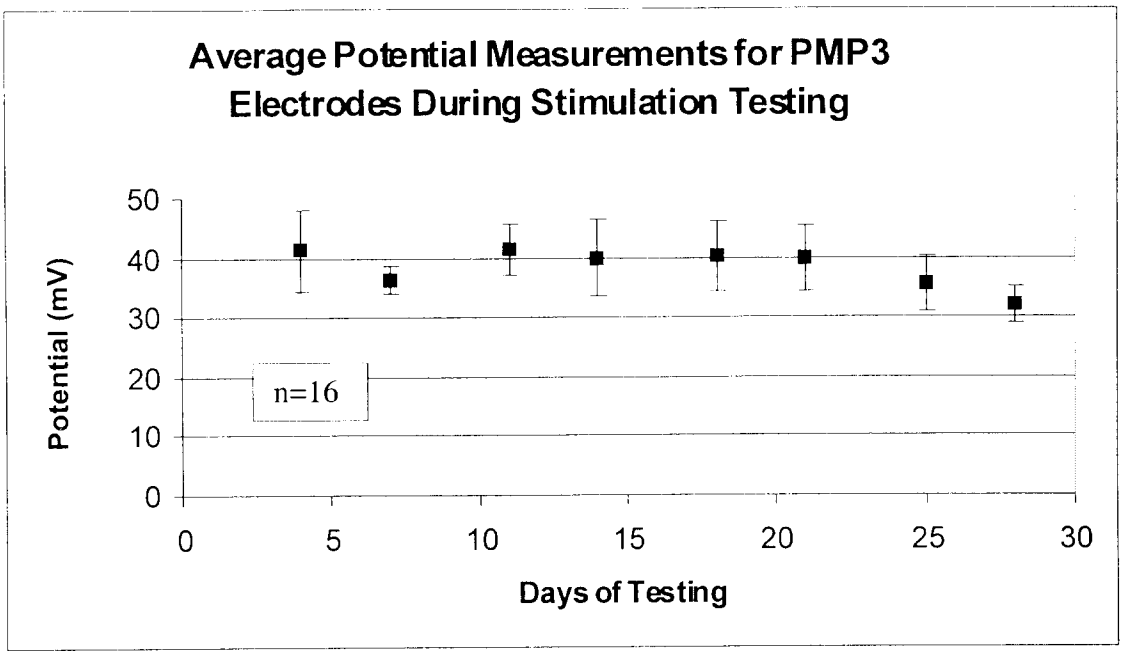

Figure B.7: Average "resting" potential for the four sites on each of the four electrodes. The average for all of the 16 stimulation sites tested is also shown. The potentials stay within a 20mV range over the 28-day period of stimulation.

The potentials recorded during the test all stayed within a 20mV range. There is no increase in the potentials over the duration of the test which supports the absorption testing and the microscopy results which reveal that there is no significant platinum loss.

B.2.6 *In Vivo* Testing

The *in vivo* testing to be performed in this contract consists of three PMP electrodes implanted in cats for 3 months each. Three PMP3 electrodes were explanted for analysis upon completion of stimulation testing performed according to Section C.I.2.2 of this report. The electrodes implanted, length of implant, cat, and recorded resistances before and after implant are displayed in the table below.

Table B.1: Resistance measurements before and after implant for the three PMP3 electrodes tested in vivo for over 35 weeks.

Electrode	Days Implanted	Cat #	Stimulation Site	Resistance (ohms) Pre-Implant	Resistance (ohms) Post-Explant
PMP3 2.8 11/23/98 1of4	257	555	0° (1)	506	505
			90° (2)	507	503
			180° (3)	505	501
			270° (4)	503	503
PMP3 2.8 11/17/98 2of2	252	576	0° (1)	486	457
			90° (2)	480	442
			180° (3)	478	439
			270° (4)	488	438
PMP3 3.0 11/17/98 1of2	244	569	0° (1)	486	X
			90° (2)	482	484
			180° (3)	510	474
			270° (4)	484	475

Note: "X" refers to a lead wire that was mistakenly cut during explant. The stimulation site in question was working properly throughout the implant. The numbers in parenthesis in the "Stimulation Site" column refer to a numbering system used during mechanical testing and SEM to differentiate the stimulation sites.

Scanning electron microscopy and elemental analysis were used to analyze the stimulation sites after explant. Elemental analysis of the stimulation sites indicated the presence of platinum, silicone, carbon, and gold. The stimulation site is platinum and the gold is explained by the gold sputter coating done to the electrodes to prepare them for SEM. The presence of carbon suggests connective tissue remaining from the implant. For most of the electrodes, the SEM picture shows a relatively clean site, yet the elemental analysis revealed significant amounts of silicone. It is believed that this is a result of the beam angle. The elemental analysis scanning beam enters the stimulation site at an angle, this could mean that the beam is picking up reflections of the silicone from the sides of the contact window. However, a few sites do have silicone visible in the site as seen in the picture below. This is believed to be due to the method of removal of the silicone. After laser machined, the silicone window is removed with forceps. Sometimes the laser does not cut all the way through and the silicone window is "torn" off with the forceps. This can leave an edge that might be susceptible to removal from the side of the site over time. Some of the SEM pictures of the sites are seen in the figures below. Plots of the elemental analysis are also shown for certain points on the sites as indicated by the small boxes on the site pictures.

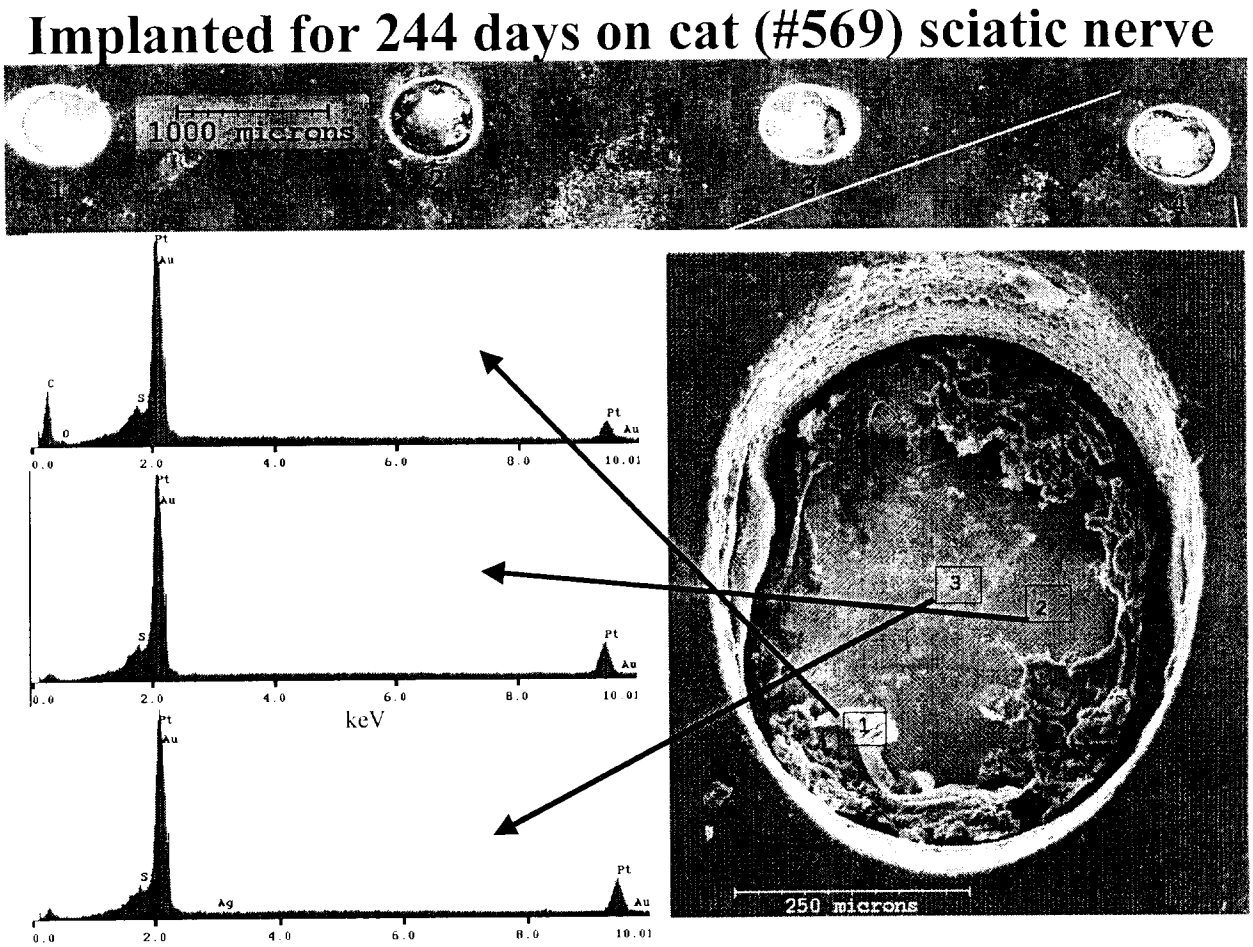

Figure B.8: The top picture is an overview of the four stimulation sites from the PMP3 electrode implanted in Cat #569. The picture on the right is site #4. There appears to be tissue around the edges of the site. Three elemental analysis scans are shown on the left. The plots correspond to the boxed numbered sites on the stimulation site. The first peak in the plot is carbon. The second peak is silicone, and the highest peaks are platinum and gold.

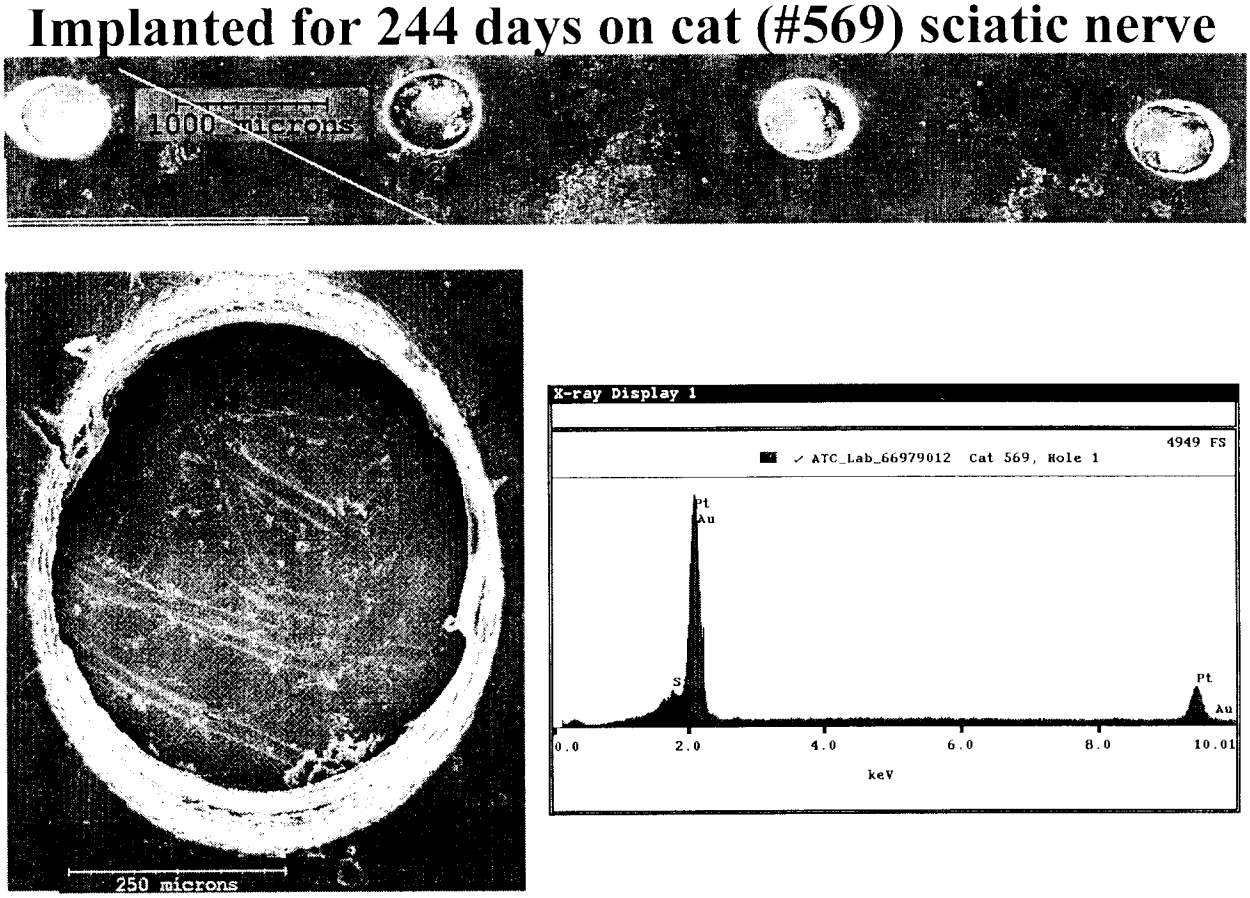

Figure B.9: The top picture is an overview of the four stimulation sites from the PMP3 electrode implanted in Cat #569. The picture on the left is site #1. This site does not appear to have tissue remnants or silicone pieces. The elemental analysis on the right confirms that there is no tissue with the very small first peak. There is still a medium sized peak for silicone. The largest peaks are platinum and gold.

The fact that there is still some silicone recorded by the elemental analysis, yet there appears to be no silicone on the site supports the idea that the scanning beam may be picking up silicone reflections from the walls of the site.

SECTION C. IN VIVO EVALUATION OF ELECTRODES

C.I.2: In Vivo Evaluation of Electrodes - Chronic Study

Abstract

The long-term effects of two types of nerve cuff electrodes, pmp and wiggle-wire electrodes, were investigated. A total of nine animals were used for this study. Four of the nine animals, of which one died on the surgical table and the other three were maintained for 30, 43 and 49 days, were previously reported on and will not be addressed in this report. The remaining five animals were maintained for 8, 8 1/2, 8 1/2, 9 1/2 and 14 months. Electrode impedance measurements were taken in each of these five cases just prior to the perfusion procedure. After the perfusion procedure, a surgical procedure was performed to remove both the right sciatic nerve with the implanted nerve cuff electrode, lead wire and tissue surrounding the exit site and the left sciatic nerve. During the surgical removal procedure, no abnormalities were noted with respect to the over all appearance of both the implanted nerve cuff electrode and the surrounding tissue.

Explant Procedure

The animals were anesthetized with a combination of Ketamine (30 mg/kg, IM), atropine (0.044 mg/kg, IM) and sodium pentobarbital (0.2 cc bolus injections, IV). Once anesthetized, the animals were intubated, and their temperature was maintained at 39° C with a thermostatically controlled heating pad. The impedance measurements were then taken (see below). Once all of the impedance measurements were taken, the animal was transferred to a respirator, and the chest was opened. Any bleeding was cauterized and the pericardium was cut away from the heart. To inhibit blood coagulation, heparin sodium (1500 units) was injected into the blood stream via hypodermic injection through the left ventricle and allowed to circulate for 2 minutes. An incision was made in the right atrium, and a tube inserted to provide a fluid drainage path for blood and perfusate. An incision was then made in the either the left ventricle of the heart or the descending aorta. A tube, through which the fixatives are were delivered, was fed through the hole and tied into place. The fixatives were pumped into the circulatory system via a peristaltic pump. First, 1 liter of warm (body temperature) saline was delivered as a pre-wash. Second 1 liter of warm (body temperature) 1% paraformaldehyde in 25 mM cacodylate buffer was delivered. Third, 1 liter of warm 3.5% glutaraldehyde in 25 mM cacodylate buffer was delivered. Finally, a second liter of glutaraldehyde was administered, cold.

Following the perfusion procedure, the sciatic nerves from both legs were dissected out of the body. An incision from the hindlimb up the length of the back was made to expose the entire length of the electrode lead. The tissue around the exit point of the lead wire was carefully excised in one unit and the lead wire with the encapsulating tissue was carefully removed from the back. The musculature of the hindlimb was carefully dissected away from the sciatic nerve with special effort to minimize any disturbance of the tissue immediately next to the sciatic nerve. Once the sciatic nerve was fully exposed, each of the branches: the common peroneal, tibial, medial gastrocnemius and the lateral gastrocnemius/soleus, were labeled with suture and cut. The sciatic nerve was cut at least a couple of centimeters proximal to the location of the nerve cuff electrode. The sciatic nerve with the nerve cuff electrode and the surrounding encapsulation tissue was then removed from the leg and place into a container filled with

glutaraldehyde. This container was then properly labeled and placed in a refrigerator for 2-3 days to allow additional fixation of the tissue. After 2-3 days the glutaraldehyde solution was removed and replaced with a sodium cacodylate buffer solution.

Impedance Measurements

The electrode impedance measurements were taken as both an indicator of any abnormalities with the electrode surface and to help develop design specifications for neural stimulators designed for implanted nerve cuff electrodes. Impedance measurements were taken for multiple electrode configurations. For every contact, a monopolar configuration was tested. This monopolar configuration consisted of using a single contact within the nerve cuff electrode with respect to a 19 guage hypodermic needle placed in the nape of the neck, which served as a distant return. Other configurations tested included the impedance across two different contacts within the cuff electrode and the impedance when multiple contacts were used in parallel with respect to the distant return. These combinations of configurations were used so that the impedance of the lead wires and body conductance (approximated to be equal for each contact) could be accounted for and the impedance of the individual electrodes could be calculated.

The experimental set-up is illustrated in Figure C.1. A stimulator was used to provide a 100 μsec monophasic pulse to the nerve cuff electrode. An oscilloscope was used to measure the resulting potentials across both the resistor and the stimulator. In each case a photograph of the oscilloscope trace was taken as a hard copy to record the data. A summary of the results for all five animals are shown in Table C.1.

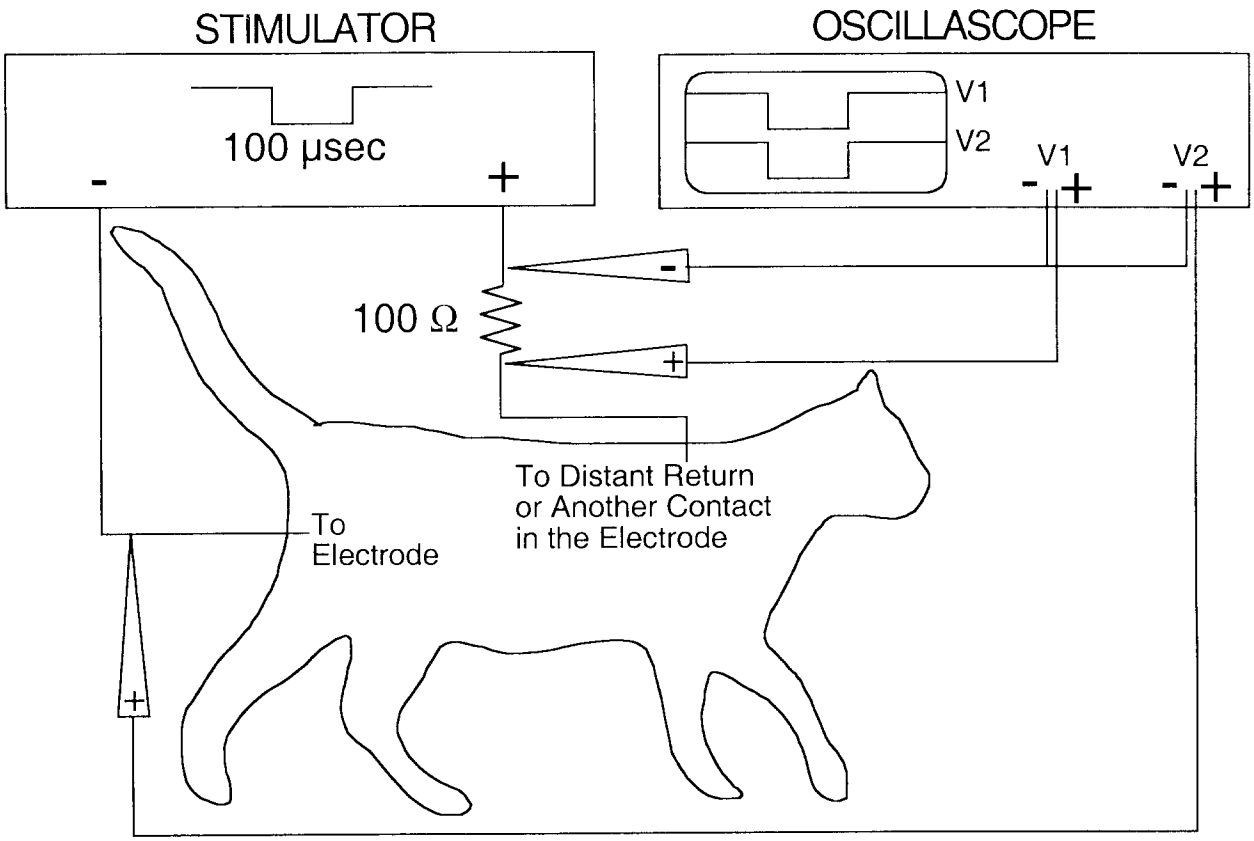

Figure C.1 - The experimental set-up used to measure the impedance of the electrodes. The stimulator provided single 100µsec monophasic pulses and the potential across both a 100 ohm resister and across the stimulator where measured with an oscillascope.

Nerve Sectioning

Each nerve was sectioned under a microscope to both identify the anatomical positions of each fascicle and to send sections for histological preparation. The nerve was spread out and firmly held in place with the aid of dissection pins. Excess fat and tissue was removed from the nerve section. The individual branches of the medial gastrocnemius, lateral gastrocnemius and the remaining tibial branch were dissected proximally to the level of the common peroneal branch point. The location of each of the contacts within the nerve cuff electrode were identified and marked with a suture tied to the nerve on each side of the cuff electrode. Each pair of suture knots were identifiable based on their color and length. The encapsulation tissue surrounding the nerve cuff electrode was then carefully cut open over the location of the lead wire in the nerve cuff electrode. The nerve cuff electrode was then carefully removed from the nerve while noting which contact location corresponded to which set of sutures place on the nerve. The contact located closest to the inside edge of the nerve cuff electrode was designated the 0° position and each subsequent contact was designated the 90°, 180° and the 270° positions respectively. Once the nerve cuff was removed the encapsulation tissue was cut circumferentially around the nerve at the center of the location where the nerve cuff was implanted. Each side of the encapsulation tissue was then folded back to expose the surface of the nerve that was in contact with the inside

of the nerve cuff electrode. On the surface of the nerve, a "bump" was typically observed where each contact was located. An example of this "bump" is illustrated in Figure C.2. This "bump" is due to the tissue filling the hole in the nerve cuff electrode which exposed the underlying contact. A line between each set of sutures, indicating the location of each contact, was then drawn using colored dye from the Davidson Marking System™ by Bradley Products, Inc. Each line was drawn using a different color to indicate its respective electrode location; the 0°, 90°, 180° and 270° contact locations were marked with red, green, blue and black dye respectively. The nerve was then cross sectioned progressively starting distally and moving proximal. At each step the arrangement of the fascicles were identified. Four sections of the nerve were taken from each nerve and sent for histological processing. The four sections included three cross sections and one longitudinal sections. The cross sections were sent for plastic embedding and include locations proximal, distal and at the center of thelocation at which the nerve cuff electrode was implanted. A longitudinal section, sent for parafin embedding, was taken through the nerve along the proximal half of where the nere cuff electrode was implanted and continued through the encapsulation tissue. An illustration of these sections are shown in Figure C.3.

Figure C.2 – An picture taken of the nerve surface where an opening for the contact had been located. A "bump" on the nerve surface is present due to the growth of tissue into the hole cut into the nerve cuff electrode to expose the electrode contact.

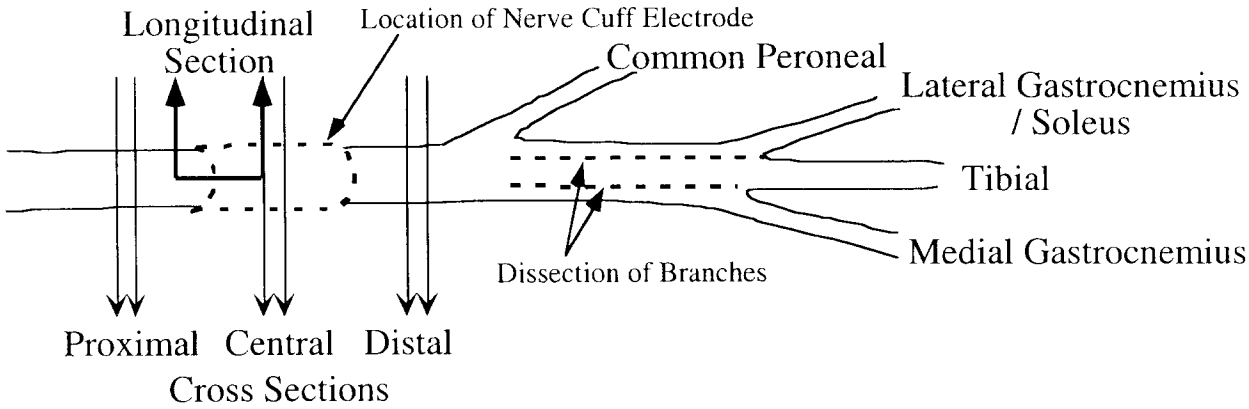

Figure C.3 – An illustration of the sciatic nerve showing the locations of sections sent for histological processing. The set of dotted lines to on the left side indicate the location at which the nerve cuff electrode was implanted. The dotted lines on the right side indicate how the individual branches were dissected up to the branch point of the common peroneal.

Cat # 399

Electrode(s)	a	b	c	d	a//b	a//c	a//d	b//c	b//d	c//d	all in //	a +c	c +d	d +a	d +b
V1 (mV)	86	90	88	85.6	86.6	88	87.6	85.6	84.8	87.2	83.8	82.4	87.6	77.4	86.6
V2 (V)	2.56	9.26	5.48	7.16	5.69	2.6	4.5	2.8	5.64	4.18	4.15	11.26	7.7	12.14	10.7
I (μA)	860	900	880	856	866	880	876	856	848	872	838	824	876	774	866
R (kohms)	2.98	10.29	6.23	8.36	6.57	2.95	5.14	3.27	6.65	4.79	4.95	13.67	8.79	15.68	12.36

Cat # 553

Electrode(s)	0	90	180	270	0//90	0//180	0//270	90//180	90//270	180//270	all in //	90 +0	180 +0	180 +90	270 +90	270 +180
V1 (mV)	84.2	88.4	84	88.6	88	84.2	88.6	87.6	85.4	88	88.6	85.2	86.8	85.6	89.8	86.2
V2 (V)	4.86	4.72	5.84	7.34	4.78	4.4	4.98	4.48	4.76	4.52	3.58	8.96	8.74	7.86	9.9	8.78
I (μA)	842	884	840	886	880	842	886	876	854	880	886	852	868	856	898	862
R (kohms)	5.77	5.34	6.95	8.28	5.43	5.23	5.62	5.11	5.57	5.14	4.04	10.52	10.07	9.18	11.02	10.19

Cat # 555

Electrode(s)	0 saturation	0 threshold	90	180	270
V1 (mV)	33.6	15.9	85	89.6	87.4
V2 (V)	10.6	4.7	7	9.95	8.6
I (μA)	336	159	850	896	874
R (kohms)	31.55	29.56	8.24	11.10	9.84

Cat # 569

Electrode(s)	0	90	180	270	270	270
V1 (mV)	83.8	82.2	84.4	51	82.4	132.5
V2 (V)	12.05	12.25	8.75	5	9.9	13.48
I (μA)	838	822	844	510	824	1325
R (kohms)	14.38	14.90	10.37	9.80	12.01	10.17

Cat # 576

Electrode(s)	a	b	c	d
V1 (mV)	23.7	44.8	85.6	89.6
V2 (V)	8.35	5.2	11.5	6.05

Table C.1 – A summary of every combination in which potential measurements were made and the calculated impedances found. A '//' is used to indicate that the two electrode contacts were used in parallel. A '+' preceding the second electrode label was used to indicate that the second electrode was used as the anode instead of the common return anode, a 19 gauge needle, placed in the nape of the neck.